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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/482,788

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BERKA

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5778.200-US

025907
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HM12/0626

EXAMINER

ART UNIT	PAPER NUMBER
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1652

DATE MAILED:

06/26/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.
09/482,788

Applicant(s)

Berka et al.

Examiner

Peter Tung

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on _____
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-3, 8, 9, 13, 22-24, 30, 31, 37, 42, 50, 53, 57-59, 63, and 64 is/are pending in the application.
- 4a) Of the above, claim(s) 30, 31, 37, 42, 50, 53, 57-59, 63, and 64 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-3, 8, 9, 13, and 22-24 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- 13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- a) ☐ All b) ☐ Some* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- *See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

- 15) ☐ Notice of References Cited (PTO-892)
- 16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 4
- 18) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 19) ☐ Notice of Informal Patent Application (PTO-152)
- 20) ☐ Other: _____

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DETAILED ACTION

Election/Restriction

1. Applicant's election with traverse of Group I, claims 1-3, 8, 9 and 13 in Paper No. 6 is acknowledged. The traversal is on the ground(s) that Group I, drawn to a method of producing heterologous polypeptides using a cyclohexadepsipeptide synthase-deficient mutant filamentous fungal cell and Group II, drawn to cyclohexadepsipeptide synthase-deficient mutant filamentous fungal cells are very related inventions and would not be a serious burden if restriction between the two groups was not required. Accordingly, Group I and Group II, claims 22-24, have been rejoined.

2. Claims 1-3, 8, 9, 13, 22-24, 30, 31, 37, 42, 50, 53, 57-59 and 63-64 are pending. Claims 30, 31, 37, 42, 50, 53, 57-59 and 63-64 are withdrawn from further consideration as being drawn to a non-elected invention.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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4. Claim 8 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

5. Claim 8 recites the limitation "mutant cell" in line 1. There is insufficient antecedent basis for this limitation in the claim.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1, 2, 8, 9, 13 and 22-24 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a *Fusarium* fungal cell producing less cyclohexadepsipeptide and a method of producing a heterologous polypeptide using said cell, does not reasonably provide enablement for any filamentous fungal cell producing less cyclohexadepsipeptide. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. Enablement requires that the specification teach those in the art to make and use the invention without undue experimentation. Factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the

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breadth of the claims. The breadth of the claims encompass any filamentous fungal cell which produces lower amounts of cyclohexadepsipeptide than a parental cell and a method of producing polypeptides using said cell. However, insufficient guidance and examples are provided of obtaining a filamentous fungal cell which produces lower amounts of cyclohexadepsipeptide from other than *Fusarium*. The relative skill of those in the art is low in making such cyclohexadepsipeptide-deficient cells in other filamentous fungi without being provided with the DNA sequences of those enzymes involved in the biosynthesis of cyclohexadepsipeptide in those particular cells. As making fungal cells with lowered levels of cyclohexadepsipeptide requires knowledge of the DNA sequences encoding enzymes involved in cyclohexadepsipeptide biosynthesis, there is unpredictability in making such cells other than in *Fusarium*, where the instant specification discloses a DNA sequence encoding a *Fusarium* cyclohexadepsipeptide synthetase. Additionally, the prior art of record does not indicate that those DNAs encoding enzymes involved in the biosynthesis of cyclohexadepsipeptide are known for other filamentous fungi besides *Fusarium*. Undue experimentation would be required to enable the full scope of the invention based upon the limited scope of the disclosure.

8. Claims 8, 9, 23 and 24 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a filamentous fungal cell which produces less cyclohexadepsipeptide and which comprises a modification of the polynucleotide sequence of SEQ ID NO: 1 and a method of producing polypeptides using said fungal cell, does not reasonably provide enablement for a filamentous fungal cell which produces less

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cyclohexadepsipeptide and which comprises a modification of at least one of the DNAs involved in the production of a cyclohexadepsipeptide and a method of producing polypeptides using said fungal cell. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. Enablement requires that the specification teach those in the art to make and use the invention without undue experimentation. Factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. The breadth of the claims encompass a fungal cell comprising a modification of at least one of the DNAs involved in the production of cyclohexadepsipeptide. However, the instant specification only discloses the DNA of SEQ ID NO: 1, which encodes a *Fusarium* cyclohexadepsipeptide synthetase. Insufficient examples and guidance are provided on other filamentous fungal DNAs involved in the production of cyclohexadepsipeptide. Besides DNA encoding *Fusarium* enniatin synthetase, the prior art of record does not teach any other DNAs encoding cyclohexadepsipeptide synthetase, enniatin synthetase or D-hydroxyisovalerate dehydrogenase. The skill of those in the art is low in making and using cyclohexadepsipeptide-deficient fungal cells without being provided the specific DNA sequence which encodes an enzyme involved in the biosynthesis of a cyclohexadepsipeptide. Absent such information, there is

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unpredictability in making fungal cells with reduced cyclohexadepsipeptide. Undue experimentation would be required to enable the full scope of the instant invention based upon the limited scope of the disclosure.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 1-3, 8, 9, 13 and 22-24 are rejected under 35 U.S.C. 102(b) as being anticipated by Herrmann et al. (cited in IDS). With regard to claims 22-24, Herrmann et al. teach (page 227, "Disruption of the esyn1 gene," 1st and 2nd paragraphs) a Fusarium comprising a disruption of the enniatin synthetase gene by hygromycin B phosphotransferase, resulting in lowered levels of cyclohexadepsipeptides. Hygromycin B phosphotransferase is heterologously expressed in the Fusarium and used as a selection marker. Claims 22-24 are therefore anticipated by Herrmann et al.

With regard to claims 1-3, 8, 9 and 13, Herrmann et al. teach (page 231, "Enzyme purification and protein blotting") isolating the heterologous polypeptide hygromycin B phosphotransferase by preparation of a crude protein extract from cyclohexadepsipeptide-deficient Fusarium, which is that of claims 1-3, 8, 9 and 13.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Peter Tung, Ph.D. whose telephone number is (703) 308-9436. The examiner can normally be reached on Monday-Friday from 9:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy, Ph.D., can be reached on (703) 308-3804. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.


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SUPERVISORY PATENT EXAMINER
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